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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,256	12/09/2003	John Gavin MacDonald	KCX-859 (19100)	4720

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DORITY & MANNING, P.A.
POST OFFICE BOX 1449
GREENVILLE, SC 29602-1449

EXAMINER	
STITZEL, DAVID PAUL	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,256	MACDONALD ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/30/04; 11/18/04;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: IDS: 1/19/05; 5/26/05; 12/12/05.

OFFICIAL ACTION

Acknowledgment of Receipt

Receipt of the Applicants' Election, *with traverse*, of Invention I, encompassing claims 1-24 and 26, which was filed on April 14, 2006, in response to the Official Action dated March 8, 2006, is acknowledged. However, Applicants have failed to provide an appropriate rebuttal as to why the Applicants are of the opinion that the Examiner's restriction requirement was improper. Applicants' unsubstantiated statement that "Applicants elect, with traverse, the species of Group I," without more, is a mere assertion and thus found unpersuasive. Therefore, since the Applicants did not distinctly and specifically point out the alleged errors in the Examiner's restriction requirement, the election has been treated as an election without traverse pursuant to MPEP § 818.03(a). As a result, the restriction requirement is deemed proper and therefore made FINAL.

Status of Claims

Claims 25 and 27 are withdrawn from further consideration as being directed to a non-elected invention. As a result, claims 1-24 and 26 are currently pending and therefore examined herein on the merits for patentability.

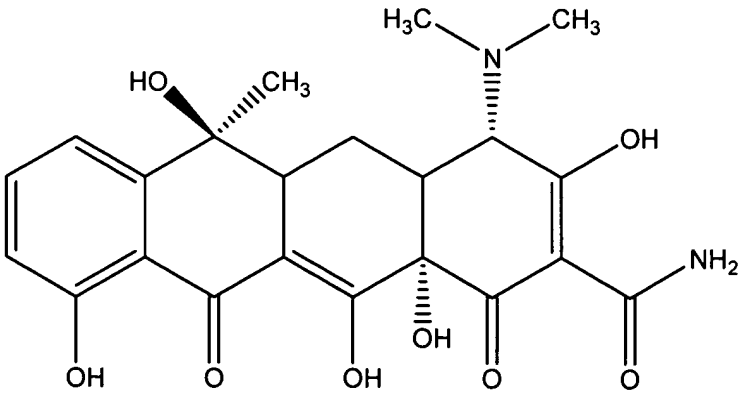
Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 102, which forms the basis of the anticipation rejections as set forth under this particular section of the Official Action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 10, 14-17, 20, 24 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 6,007,795 (hereinafter the Masterman '795 patent).

With respect to claims 1-7, 10, 14-17, 20, 24 and 26 of the instant application, the Masterman '795 patent discloses a method for treating a bacterial infection by inhibiting bacteria in an oral and/or gastrointestinal cavity of a patient comprising: (a) providing a particle comprising: a degradable inorganic composite arranged on a surface of said particle; and a tetracycline antimicrobial agent adsorbed, or chemically bound, to said degradable inorganic composite, wherein said degradable inorganic composite is selected from alumina and silica; (b) placing said particle into said oral and/or gastrointestinal cavity of said patient via a vehicle selected from a liquid (i.e., oral rinse/mouthwash) and a gel (i.e., toothpaste); and (c) exposing said particle to mechanical stresses (i.e., chewing, brushing and flossing), salivary enzymes, and gastrointestinal acidic pH, whereby said tetracycline antimicrobial agent (the molecular structure of which is illustrated hereinbelow) is desorbed from said degradable inorganic composite arranged on said surface of said particle, and thereby released into said oral and/or gastrointestinal cavity of said patient (abstract; column 1, lines 10-13 and 37-67; column 2, lines 1-13, 20, 27-31 and 41-54; column 3, lines 1-9 and 54-67; column 4, lines 64-67; column 5, lines 1-9 and 33-55):



Tetracycline

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

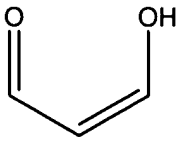
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-8, 10-18, 20-24 and 26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pre-Grant Patent Application Publication 2003/0082237 (hereinafter the Cha '237 publication) in view of The Merck Index, 10th Edition, p. 104, 408, 499, 1199 and 1200 [Antimycin A_1 Monograph No. 739; Daunorubicin Monograph No. 2815; Doxorubicin Monograph No. 3435; Salicylanilide Monograph No. 8188] (1983) (hereinafter the Merck Index publication).

With respect to claims 1-8, 10-18, 20-24 and 26 of the instant application, the Cha '237 publication teaches a method for targeted delivery of a pharmaceutical agent and/or a nutraceutical to a site specific location (i.e., arterial, tumor, vagina, or gastrointestinal tract) within a patient comprising: (a) providing a microsphere delivery device comprising a shell substrate consisting of a plurality of

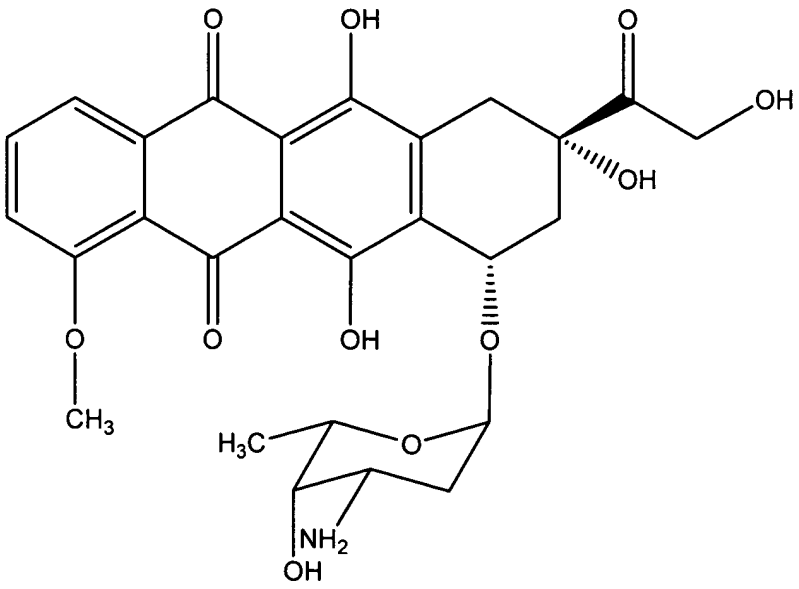
inorganic metal oxide (i.e., aluminum oxide and silicon oxide) nanoparticles, the surface of which are functionalized by the attachment of a pharmaceutical agent (i.e., chemotherapeutic agents and fungicides) and/or a nutraceutical (i.e., dye); (b) placing said particle into said site specific location of said patient; and (c) exposing said particle to pH gradients and/or salt gradients, whereby said pharmaceutical agent and/or nutraceutical is thereby released into said artery, tumor, vagina or gastrointestinal tract of said patient (abstract; [0004]; [0005]-[0010]; [0020]; [0021]; [0024]; [0025]; [0028]; [0040]-[0045]; [0055]; [0056]; [0060]-[0065]; [0078]; [0080]; [0089]; [0090]; [0093]; [0098]-[0102]; [0108]-[0111]; [0113]).

The Cha '237 publication does not explicitly teach that said pharmaceutical agent (i.e., chemotherapeutic agents and fungicides) and/or said nutraceutical (i.e., dye) comprises a chemical moiety (the molecular structure of which is illustrated hereinbelow), as claimed in claims 4, 5, 15 and 26 of the instant application:

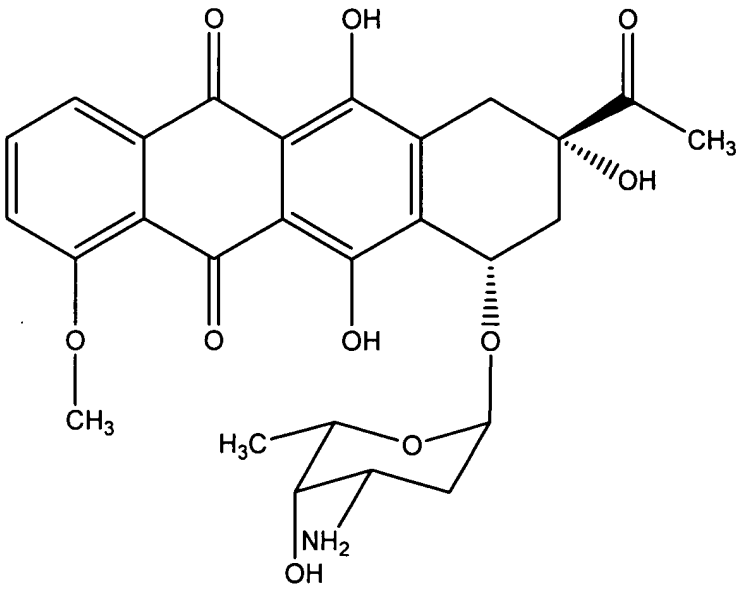


However, the Cha '237 publication teaches a drug delivery system comprising a pharmaceutical agent (i.e., chemotherapeutic agent) and/or a nutraceutical (i.e., dye), such as doxorubicin and daunorubicin ([0010]). Furthermore, the Merck Index publication not only teaches that doxorubicin and daunorubicin are antineoplastic chemotherapeutic agents (the molecular structures of which are illustrated hereinbelow), but also teaches that daunorubicin is a pH sensitive dye that changes color from pink at an acidic pH to blue at an alkaline pH. It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate doxorubicin and/or daunorubicin as the pharmaceutical agent (i.e., chemotherapeutic

agent) and/or nutraceutical (i.e., dye) taught in the method of the Cha '237 publication, since the Merck Index publication not only teaches that doxorubicin and daunorubicin are antineoplastic chemotherapeutic agents (the molecular structures of which are illustrated hereinbelow), but also teaches that daunorubicin is a pH sensitive dye that changes color from pink at an acidic pH to blue at an alkaline pH. One of ordinary skill in the art at the time the instant application was filed would have been motivated to incorporate doxorubicin and/or daunorubicin as the pharmaceutical agent (i.e., chemotherapeutic agent) and/or nutraceutical (i.e., dye) taught in the method of the Cha '237 publication, because the Cha '237 publication explicitly teaches incorporating chemotherapeutic agents and dyes, namely doxorubicin and daunorubicin, into drug delivery systems.



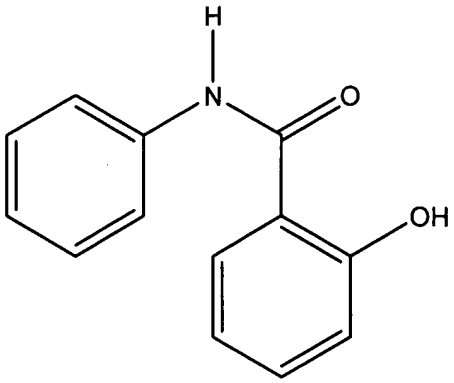
Doxorubicin



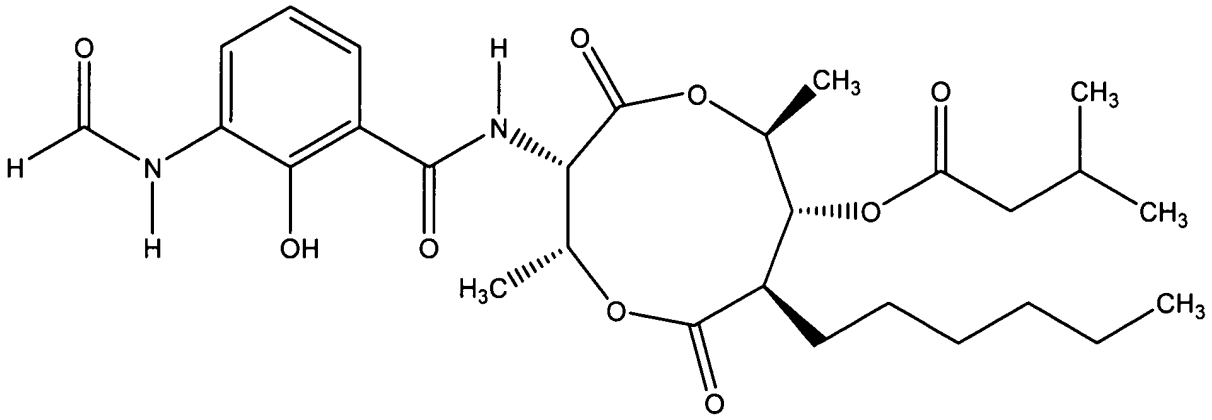
Daunorubicin

In addition, the Cha '237 publication teaches a drug delivery system comprising a pharmaceutical agent, such as a fungicide. Furthermore, the Merck Index publication teaches utilizing salicylanilide and antimycin A_1 as fungicides. It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate salicylanilide and/or antimycin A_1 as the fungicide taught in the the Cha '237 publication, since the Merck Index teaches that salicylanilide and antimycin A_1 are particularly useful as fungicides. One of ordinary skill in the art at the time the instant application was filed would have been motivated to incorporate salicylanilide and/or antimycin A_1 as the fungicides taught in the Cha '237 publication, since the Merck Index publication reasonably suggests utilizing salicylanilide and antimycin A_1 as fungicides. One of ordinary skill in the art at the time the instant application was filed would have had a reasonable expectation of success in incorporating salicylanilide and/or antimycin A_1 (the molecular structures of which are illustrated hereinbelow) as the fungicides taught in the Cha '237 publication, since the

Merck Index is the quintessential reference manual with respect to selecting specific organic chemical compounds based on their particularly disclosed therapeutic use.



Salicylanilide



Antimycin A_1

With respect to claims 11-13 and 21-23 of the instant application, although the Cha '237 publication teaches that said pharmaceutical agent and said nutraceutical are desorbed from said microsphere delivery device upon exposure to pH gradients ([0099]; [0133]), the Cha '237 publication

fails to explicitly teach desorbing said pharmaceutical agent and said nutraceutical from said microsphere delivery device by changing the environmental pH either from an alkaline pH to an acidic pH, or from an acidic pH to an alkaline pH, and particularly an alkaline pH of between 9 and 10, as claimed in claims 11-13 and 21-23 of the instant application. However, while the Cha '237 publication does not explicitly teach desorbing said pharmaceutical agent and said nutraceutical from said microsphere delivery device by changing the environmental pH either from an alkaline pH to an acidic pH, or from an acidic pH to an alkaline pH, and particularly an alkaline pH of between 9 and 10, as instantly claimed, it is well within the purview of the skilled artesian to determine the optimal pH gradient modifications for desorbing said pharmaceutical agent and said nutraceutical from said microsphere delivery device, by systematically adjusting the environmental pH during the course of routine experimentation. One of ordinary skill in the art at the time the instant application was filed would have been motivated to systematically adjust the environmental pH during the course of routine experimentation so as to obtain effective desorption of said pharmaceutical agent and said nutraceutical from said microsphere delivery device. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 105 USPQ 233, 235 (CCPA 1955). "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." See *Peterson*, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

2. Claims 9 and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Cha '237 publication in view of U.S. Pre-Grant Patent Application Publication 2003/0099718 (hereinafter the Burrell '718 publication).

The teachings of the Cha '237 publication are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

The Cha '237 publication does not explicitly teach incorporating said microsphere delivery device, which comprises said plurality of inorganic nanoparticles, into a transdermal drug delivery device, as claimed in claims 9 and 19 of the instant application. However, the Burrell '718 publication teaches incorporating an antimicrobial nanocrystalline powder into a transdermal patch for treating bacterial infections of mucosal membranes within oral, vaginal and gastrointestinal cavities (abstract; [0009]; [0027]; [0063]-[0066]; [0070]; [0071]; [0146]). It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the method of the Cha '237 publication, by incorporating said plurality of inorganic nanoparticles into a transdermal drug delivery device, as reasonably suggested by the Burrell '718 publication. One of ordinary skill in the art at the time the instant application was filed would have been motivated to incorporate the plurality of inorganic nanoparticles taught in Cha '237 publication into a transdermal drug delivery device, so as to provide a transdermal patch for the effective treatment of bacterial infections of mucosal membranes within oral, vaginal and gastrointestinal cavities, as reasonably suggested by the Burrell '718 publication.

3. Claims 8, 9, 18 and 19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Masterman '795 patent in view of U.S. Pre-Grant Patent Application Publication 2003/0099718 (hereinafter the Burrell '718 publication).

The teachings of the Masterman '795 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

The Masterman '795 patent does not explicitly teach incorporating said particles, which have an antimicrobial agent adsorbed to the surface thereof via an inorganic composite, into a transdermal drug delivery device for application into a body cavity, as claimed in claims 8, 9, 18 and 19 of the instant application. However, the Burrell '718 publication teaches incorporating an antimicrobial nanocrystalline powder into a transdermal patch for treating bacterial infections of mucosal membranes within oral, vaginal and gastrointestinal cavities (abstract; [0009]; [0027]; [0063]-[0066]; [0070]; [0071]; [0146]). It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the method of treating a bacterial infection in an oral and/or gastrointestinal cavity taught in the Masterman '795 patent, by incorporating the particles of the Masterman '795 patent into a transdermal drug delivery device, as reasonably suggested by the Burrell '718 publication. One of ordinary skill in the art at the time the instant application was filed would have been motivated to incorporate the particles taught in Masterman '795 patent into a transdermal drug delivery device, so as to provide a transdermal patch for the effective treatment of bacterial infections of mucosal membranes within oral and gastrointestinal cavities, as reasonably suggested by the Burrell '718 publication.

Conclusion

Claims 1-24 and 26 are rejected because the claimed invention would have been anticipated and/or prima facie obvious to one of ordinary skill in the art at the time the invention was made since each and every element of the claimed invention, as a whole, is disclosed in and/or would have been reasonably suggested by the teachings of the cited prior art references.

Remarks

The following is a list of patents and patent publications, both foreign and domestic, made of record and considered pertinent to the Applicants' disclosure, but are not however currently relied upon in construing the claim rejections as set forth herein:

- U.S. Patent 5,314,855 (the Thorpe '855 patent);
- U.S. Patent 5,616,315 (the Masterman '315 patent);
- U.S. Patent 5,858,503 (the Everhart '503 patent);
- U.S. Patent 5,998,222 (the Weimer '222 patent);
- U.S. Patent 6,200,555 (the Nishijima '555 patent);
- U.S. Patent 6,210,625 (the Matsushia '625 patent);
- U.S. Patent 6,277,489 (the Abbott '489 patent);
- U.S. Patent 6,361,780 (the Ley '780 patent);
- U.S. Patent 6,432,872 (the Tsushio '872 patent);
- U.S. Patent 6,589,562 (the Shefer '562 patent);
- U.S. Pre-Grant Patent Application Publication 2002/0149656 (the Nohr '656 publication);
- U.S. Pre-Grant Patent Application Publication 2003/0203991 (the Schottman '991 publication);
- U.S. Pre-Grant Patent Application Publication 2004/0120904 (the Lye '904 publication); and
- International Patent Application Publication WO2004/060378 (the Lye '378 publication).

Contact Information

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to David P. Stitzel, M.S., Esq., whose telephone number is 571-272-8508. The Examiner can normally be reached on Monday-Friday, from 7:30AM-6:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Johann Richter, Ph.D., Esq., can be reached at 571-272-0646. The central fax number for the USPTO is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published patent applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished patent applications is only available through Private PAIR. For more information about the PAIR system, please see http://pair-direct.uspto.gov. Should you have questions about acquiring access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David P. Stitzel, M.S., Esq.
Patent Examiner
Technology Center 1600
Group Art Unit 1616
May 2, 2006

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
Technology Center 1600
Group Art Unit 1616